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Adapt or Die

One Enzyme Fits All

by Malcolm Campbell

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Abstract

Most teaching labs seem to have been designed in a vacuum. To unify teaching labs, choose one model enzyme for students to study in depth in all its biological contexts, from enzymology to genetics to ecology.

The IDH enzyme gives our lab courses greater context.

Can you guess what amylase, acid phosphatase, and *Drosophila* eye color have in common? You probably can't unless you teach biology. The answer is that all three are used in teaching labs. Since the very first such labs were created, students have had to perform experiments on "model" systems that were totally unrelated to each other. Although many educators are trying to revise the biology curriculum, little of that attention has been focused on the laboratory curriculum. Typically, each lab course is designed in a vacuum, with little concern for the content in other lab courses.

At Davidson College, we have initiated a coordinated effort to unify our laboratory curriculum; our efforts have been recognized as exceptional by the National Science Foundation, which recently awarded us an Instrumentation and Laboratory Improvement grant. We chose a model enzyme, isocitrate dehydrogenase (IDH), to be used in as many laboratory courses as possible (figure 1). We have developed laboratory modules in introductory biology, molecular biology, and biochemistry, which are all freely available from our IDH Web page; protocols for genetics and developmental biology are under way.

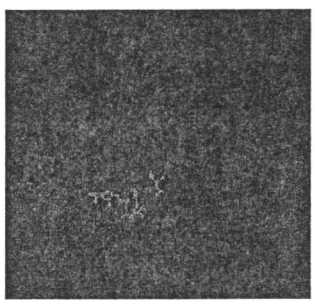

Figure 1

There are three IDH genes in most eukaryotes. The most familiar one is an NAD^+-dependent enzyme located in mitochondria. A second form found in the mitochondria is dependent on $NADP^+$ rather than NAD^+ [1]. We use the third form, which is very abundant, $NADP^+$ dependent, located in the cytoplasm, and involved in lipid synthesis. The atomic structure has been determined for IDH from several species and with different other molecules bound. One can locate files on our IDH Web site, viewable with freeware such as RasMol, Chime, or Cn3D; you can find your own RasMol images through the National Center for Biotechnology Information Structure Group. These files of X-ray crystallography data allow students to interactively view the enzyme bound to its substrate (isocitrate), its coenzyme ($NADP^+$), and its cofactor (Mg^{2+})

[2].

Studied in introductory courses and safe to assay, IDH is an ideal enzyme.

Students are introduced to IDH during their first introductory course on cell and molecular biology. They perform a series of three experiments that introduce them to spectrophotometric methods and enzyme kinetics. For their third lab, they perform an experiment of their own design to test a hypothesis of their choosing. Traditionally, students worked with tyrosinase, peroxidase, or acid phosphatase. These enzymes are unsatisfactory for two main reasons: (1) They use toxic reagents as a part of the enzyme assay, and (2) they are not discussed in lecture because they are not mainstream proteins. In contrast, IDH activity can be measured spectrophotometrically by determining the concentration of the product NADPH by light absorption at 340 nm. Furthermore, IDH is part of a metabolic pathway that is discussed in most introductory courses.

We want students to benefit in upper-level courses from what they learn during introductory labs. In biochemistry lab, students purify and characterize IDH. The enzyme is easy to prepare from almost any animal or plant source, and students can compare specific activities of different species or of tissues from the same species. They can examine holoenzyme and subunit sizes or whether their isolated enzyme can utilize NAD^+ and/or $NADP^+$. In molecular biology lab, students start by utilizing yeast genome data from the *Saccharomyces* Genome Database. They search the database for the IDH gene, design polymerase chain reaction primers, and amplify, clone, and express the yeast IDH gene in bacteria. The recombinant protein is functional and has a short epitope tag attached so that it can be detected on an immunoblot. Finally, students can use their cloned yeast gene as a probe on a Southern blot with DNA isolated from a wide range of species.

IDH can be revisited in upper-level lab courses, from genetics to ecology.

We are developing a genetics lab module in which students will use null alleles of IDH to examine inheritance patterns in *Drosophila* . This can be combined with enzyme assays and linkage analysis to provide an investigatory lab module. Students taking a course in development will examine the time and location of IDH gene expression in model embryos such as chicken, fish, flies, worms, and sea urchins. Because enzyme activity can be detected colorimetrically, students will be able to visualize a process that is normally discussed but not seen directly: gene regulation of when and where IDH is expressed. Other courses could be affected as well. Ecology students could determine the isozyme genotypes of a population using starch gel electrophoresis. Those studying physiology could explore the effects different isozymes might have on function at the tissue or organism level. Students of immunology could produce antibodies against IDH, and those studying cell biology could use immunologic or centrifugation methods to determine the subcellular localization of IDH. Cell biology students could use different signal peptides to target the same enzyme to different organelles. The only limitation is the imagination of the faculty.

Both students and faculty benefit from using a single enzyme in different courses. Students learn that the separations between laboratory courses are artificial boundaries that do not reflect the continuum of biology. There is a reward for learning about an enzyme covered in their first laboratory course and an incentive for carrying over learned information from one lab to others. Faculty members benefit when they collaborate on the development of new labs; senior members bring years of experience with different organisms, while junior members bring newer methods, so they can be equal partners. Working with colleagues on a common goal is a good way to generate renewed enthusiasm and to foster teamwork and mutual respect among the faculty. As new laboratory modules are developed, the team can publish its results in a peer-reviewed teaching journal such as American Biology Teacher, Bioscene: Journal of College Biology Teaching, Biochemical Education, or Journal of College Science Teaching. When students see a cohesive faculty, they view the curriculum as more cohesive, too.

In short, adopting a model enzyme such as IDH presents a win-win learning environment. Our IDH lab protocols are all freely available from the IDH home page. New IDH-based protocols will be developed over the next few years as more courses and faculty embrace a unified laboratory curriculum.

A. Malcolm Campbell is an assistant professor of biology at Davidson College. He has made numerous presentations about teaching as an "alternative" career option, and has written How to Get a Teaching Job at a Primarily Undergraduate Institution .

Andrzej Krauze is an illustrator, poster maker, cartoonist, and painter who illustrates regularly for HMS Beagle, The Guardian, The Sunday Telegraph, Bookseller , and New Statesman.

Endlinks

Association for Biology Laboratory Education - provides links to interesting and innovative laboratory exercises, conferences, workshops, and related Internet resources.

Biolab Home Page - an unmoderated email list for discussion of issues and information related to teaching college biology laboratories.

Beyond Bio101: The Transformation of Undergraduate Biology Education - a report from the Howard Hughes Medical Institute describing remarkable changes taking place in how American college students learn biology.

CSU Bioweb - California State University's site consolidates biological science teaching and research resources.

NABT Online Resources - the National Association of Biology Teachers collection of links for biology teachers.

Federal Resources for Educational Excellence - provides access to hundreds of free teaching and learning resources throughout the federal government.

Model Systems - an HMS *Beagle* Cutting Edge Dialogue.

Tell us what you think.

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